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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/517,741	01/03/2006	John Foekens	47675-93	8977

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EXAMINER	
MYERS, CARLA J	

ART UNIT	PAPER NUMBER
1634	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/517,741	FOEKENS ET AL.	
	Examiner	Art Unit	
	Carla Myers	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 May 2009 and 27 May 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,20-24,45,57-59,61,62,67 and 77* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,20-24,45,57-59,61,62,67 and 77* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/27/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This action is in response to the reply of May 27, 2009. Applicant's arguments and amendments to the claims have been fully considered but are not persuasive to place all claims in condition for allowance. All rejections not reiterated herein are hereby withdrawn. In particular, the objection to the specification is withdrawn in view of the amendment to the specification to add the title "Brief Description of the Drawings" and to amend the description of Figures 6, 8, 10 and 12. The rejection of claims 20, 45, 57-59, 61, 62, 67 and 77 under 35 U.S.C. 112, second paragraph has been obviated by the amendment to the claims.

2. Claims 1, 20-24, 45, 57-59, 61, 62, 67 and 77 are pending and have been examined herein.

3. The following are new grounds of rejection necessitated by Applicant's amendments to the claims.

Claim Rejections - 35 USC § 112 second paragraph

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 20-24, 45, 57-59, 61, 62, 67 and 77 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 20-24, 45, 57-59, 61, 62, 67 and 77 are indefinite over the recitation of "selected from the group consisting of essentially" because the claim recites an improper format for a Markush group. Claims which recite members of a Markush

group must be 'close-ended'. It is noted that The MPEP (2111.03 – Transitional phrases) indicates that:

> A 'consisting essentially of' claim occupies a middle ground between closed claims that are written in a consisting of' format and fully open claims that are drafted in a comprising' format." PPG Industries v. Guardian Industries, 156 F.3d 1351, 1354, 48 USPQ2d 1351, 1353-54 (Fed. Cir. 1998). See also Atlas Powder v. E.I. duPont de Nemours & Co., 750 F.2d 1569, 224 USPQ 409 (Fed. Cir. 1984); In re Janakirama-Rao, 317 F.2d 951, 137 USPQ 893 (CCPA 1963); Water Technologies Corp. vs. Calco, Ltd., 850 F.2d 660, 7 USPQ2d 1097 (Fed. Cir. 1988). For the purposes of searching for and applying prior art under 35 U.S.C. 102 and 103, absent a clear indication in the specification or claims of what the basic and novel characteristics actually are, "consisting essentially of" will be construed as equivalent to "comprising."

However, the present claims do not recite the language "consisting essentially of" but rather recite "consisting of essentially," thereby further compounding the indefiniteness of the claim. Note that the phrase "consisting of essentially" has not been clearly defined in the specification or claims. Further, it is noted that MPEP 2173.05(h) states that "It is improper to use the term "comprising" instead of "consisting of" when reciting a Markush group. Ex parte Dotter, 12 USPQ 382 (Bd. App. 1931).") This rejection may be overcome by amendment of the claim to recite "selected from the group consisting of".

Claim Rejections - 35 USC § 112 – New Matter

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 20-24, 45, 57-59, 61, 62, 67 and 77 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a

way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

The specification as originally filed does not appear to provide support for the amendment to the claims to recite that hypomethylation of PITX2 is indicative of low risk for relapse and that hypermethylation of PITX is indicative of high risk for relapse.

The response states that support for the amendment is found at pages 58 and 59 and Figure 19. However, pages 58 and 59 provide only a listing of primers used to amplify genes, including the PITX2 gene. Figure 19 "shows the Kaplan-Meier estimated disease-free survival curves for the gene PITX2" (page 35). It is noted that in the response of May 26, 2009, Applicants amended the description of Figure 19 to indicate that the upper dotted line shows responders and the lower unbroken line shows non-responders. However, Figure 19 does not provide any information to indicate the hypomethylation or hypermethylation status of the responders or non-responders. Further, this figure provides information regarding only time of disease-free survival. This is not equivalent to teaching that hypomethylation is correlated with low risk of relapse and that hypermethylation is correlated with high risk of relapse.

Maintained Rejections

Claim Rejections - 35 USC § 112 - Enablement

6. Claims 1, 20-24, 45, 57-59, 61, 62, 67 and 77 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable

one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

This rejection was previously set forth in the Office action of November 24, 2008 and is maintained for the reasons set forth therein.

Response to Remarks:

In the response of May 26, 2009, Applicants state that the claims have been amended so that they are limited to human subjects. However, claims 62, 67 and 77 have not been amended so that they are limited to human subjects. Rather, the claims broadly recite the analysis of "subjects" and thereby encompass the analysis of any human or non-human subjects, including rats, dogs, horses, pigs, pandas etc.

The response states that the claims have been amended to recite "therapeutic treatment" in place of "therapy." The response does not indicate how this amendment is intended to address the 112, first paragraph rejection. The phrase "therapeutic treatment" has not been defined in the specification or claims in any manner which would limit the claims to any particular type of therapeutic treatment. The claims still encompass methods which predict a response to any therapeutic treatment with a drug that targets any component of the estrogen receptor pathway or drugs that are involved in estrogen metabolism, production or secretion. The drug may be an adjuvant treatment or a primary therapy. Thereby, the claims encompass determining responsiveness to a very wide range of drugs (antisense drugs, ribozymes, antibody therapy, organic and inorganic compounds), which differ in their structure and mechanism of action. The response fails to provide any evidence to establish that

hypermethylation or hypomethylation of PITX2, related genes or genes contiguous (upstream or downstream) of PITX2 is correlated with response to a representative number of such diverse therapeutic treatments.

The response points to pages 58 and 59 of the specification and Figure 19 as showing that the hypermethylation of PITX2 is correlated with survival of patients. Applicants note that they amended the description of Figure 19 because they previously incorrectly labeled the lines for responders and non-responders. It is asserted that Example 1, Data set 2 (adjuvant therapy) provides evidence that the specified coefficient of the Cox model for PITX2 indicates that hypermethylation of PITX2 is correlated with increased risk of relapse.

These arguments have been fully considered but are not persuasive. Pages 58 and 59 of the specification are limited to a Table which provides the sequences of primers. These pages do not provide any information regarding a correlation between PTIX2 methylation status and response to therapeutic treatment. The section of the specification entitled "Data set 2: Adjuvant Setting" (pages 44-45) states only that "Every CpG was put into a Cox proportional hazard model together with the known predictive markers N-stage and tumour size. The best marker was the gene PITX2." It is also stated that the oligonucleotide number 3522:2087 "gives information about survival time independent of nStage. The tumour size has no significant predictive power for expected survival time." However, the specification does not indicate whether hypermethylation or hypomethylation was correlated with survival time. Note that Figure 19 includes two lines – responders and non-responders. However, Figure 19 does not

state which line represents hypermethylation or hypomethylation of any particular PITX2 sequence. Moreover, the present claims are directed to a method that predicts risk of relapse, not survival time. The specification does not teach that survival time is a measure of the risk of relapse per se, particularly as it pertains to any type of therapy. Further, this data appears to be limited to only adjuvant therapy. At page 43, under the section entitled "Data set 1: Adjuvant setting", it is stated that the methylation patterns were obtained from patients treated with Tamoxifen as an adjuvant following therapy. It is unclear as to this is the same type of therapy that was used for the patients studied in data set 2. Also, the information provided in this example cannot be properly evaluated because the example does not provide any information regarding the number of patients analyzed, the type of treatment, the disorder that the patients were treated for, the age or sex of the patients, etc. Additionally, the information provided at page 45 is limited to a single fragment of the PITX2 gene (oligonucleotide "3522:2087") and the specification does not appear to provide any information as to the identity of this particular sequence (e.g., its location within the PITX2 gene, its length etc). There is no information regarding the methylation status of other PITX2 gene sequences.

Regarding the fact that the claims broadly encompass predicting responsiveness of a subject with any breast tissue cell proliferative disorder, Applicants state that he claims are limited to a subclass of breast cancer namely estrogen receptor positive cells. This argument is not persuasive because the present claims are not in fact limited to breast cancers characterized by estrogen receptor positive cells.

The response further states that the subclassification of breast cancer into subtypes is irrelevant for clinical implications and point to Sorlie (2001) and Perou (2001) in support of this argument, stating that breast tissue cells all originate from a common source.

This argument has also been fully considered but is not persuasive. First, it is noted that the claims are not limited to breast cancer, but rather are broadly drawn to predicting responsiveness of a subject with any breast tissue cell proliferative disorder. Secondly, the cited prior art of Sorlie in fact supports the unpredictability in the art. Sorlie teaches that gene expression patterns vary with tumor subclasses and particularly teaches that there are at least two subclasses of estrogen responsive breast cancers, each having a different gene expression pattern. Given that gene expression patterns can reflect differences in methylation patterns, the teachings of Sorlie indicate that one would expect to observe variation in the gene expression patterns of different breast cancer types, and particularly even within subclasses of estrogen receptor positive breast cancers. Similarly, the teachings of Perou also support the unpredictability of extrapolating the results obtained with one type of breast tumor to other types of breast tumors. Perou teaches that "human breast tumours are diverse in their natural history and their responsiveness to treatment. Variation in transcriptional programs accounts for much of the biological diversity of human cells and tumors...Here we have characterized variation in gene expression patterns in a set of 65 surgical specimens of human breast tumors from 42 different individuals, using complementary DNA microarrays representing 8,102 human genes. These patterns provided a

distinctive molecular portrait of each tumour...The tumours could be classified into subtypes distinguished by pervasive differences in their gene expression pattern" (see abstract). Thereby, the fact that all types of breast cancer originate from a common source of breast tissue cells does not permit one to reasonably predict the methylation pattern of various types of breast cancer. There is no evidence provided in the specification to support a conclusion that the results obtained with one type of breast cancer can be extrapolated to all other types of breast cancer (benign, metastatic, estrogen receptor negative, etc), or to all other types of breast tissue cell proliferative disorders.

Applicants state that regarding the Martens and Nimmrich papers, the "Examiner has not presented any reason why these papers should preclude patentability of the presently amended claims."

However, Martens and Nimmrich were cited to establish the unpredictability in the art. Again, Martens et al teaches the results of a study of the methylation status of 117 genes, including the PITX2 gene, in 200 steroid hormone receptor responsive tumors in patients who received tamoxifen as first-line treatment for recurrent breast cancer. **Martens did not observe an association between response to treatment and methylation status of PITX2** (see Supplemental Tables 1 and 2). The findings of Martens contradict the conclusion set forth in the present claims that hypomethylation of PITX2 is associated with low risk of relapse and hypermethylation is associated with high risk or relapse of any type of breast proliferative disorder following any type of therapeutic treatment with a drug that targets an estrogen receptor pathway or is in

some manner involved in estrogen metabolism, production or secretion. Thereby, the findings of Martens are clearly relevant to the presently claimed invention.

The teachings of Nimmrich also establish the unpredictability in the art. Again, Nimmrich states that in the previous retrospective study of Martens, "we did not find DNA-methylation of PITX2 of the primary tumor to be associated with tamoxifen response (given as a first-line single endocrine agent) in metastatic breast cancer. " It is noted that in a subsequent study Nimmrich analyzed DNA-methylation of the PITX2 gene in untreated lymph node-negative hormone receptor positive breast cancer patients and found that hypermethylation of PITX2 was associated with a poor prognosis and disease progression in these patients. However, Nimmrich clarifies the distinction between a marker that is prognostic and markers that are predictive of response to treatment, stating that "a prognostic factor is not necessarily also a predictive marker, or vice versa" (page 434). Nimmrich teaches that differences in methylation results may occur between early stage and advanced breast cancer due to the differences in tumor biology (page 434). The teachings of Nimmrich support the unpredictability of extrapolating the results obtained with one type of breast tissue proliferative disorder to other types of breast tissue proliferative disorders (e.g., early stage breast cancer as compared to late stage, metastatic breast cancer), and with one type of therapy to other types of therapy (e.g., primary treatment with tamoxifen as compared to adjuvant treatment of recurrent cancer with tamoxifen).

Applicants state that the claims are limited to the analysis of "SEQ ID NO: 83, 411, 412, 685, 686, complementary sequences or contiguous portions thereof." It is

asserted that complementarity refers to complete complementarity. It is stated that the claims are commensurate in scope with respect to the PITX2 gene.

These arguments have been fully considered but are not persuasive. First, it is noted that the response does not address how the phrase "contiguous" sequences limits the claims to PITX gene sequences. Sequences contiguous with SEQ ID NO: 83, 411, 412, 685 and 786 include any sequences that are at any distance upstream or downstream of the recited sequences and thereby includes sequences in genes other than PITX2. Secondly, the term "complementary" has not been defined in the specification as being limited to sequences fully complementary to the recited sequence. There is also no art recognize definition for the term "complementary" which limits the term to only sequences that share full/100% complementarity. Rather, the term is broadly used in the art to indicate a degree of complementarity shared between sequences. For instance, Schlegel et al (U.S. Patent No. 7,125,663) states that:

> Complementary" refers to the broad concept of sequence complementarity between regions of two nucleic acid strands or between two regions of the same nucleic acid strand. It is known that an adenine residue of a first nucleic acid region is capable of forming specific hydrogen bonds ("base pairing") with a residue of a second nucleic acid region which is antiparallel to the first region if the residue is thymine or uracil. Similarly, it is known that a cytosine residue of a first nucleic acid strand is capable of base pairing with a residue of a second nucleic acid strand which is antiparallel to the first strand if the residue is guanine. A first region of a nucleic acid is complementary to a second region of the same or a different nucleic acid if, when the two regions are arranged in an antiparallel fashion, at least one nucleotide residue of the first region is capable of base pairing with a residue of the second region. Preferably, the first region comprises a first portion and the second region comprises a second portion, whereby, when the first and second portions are arranged in an antiparallel fashion, at least about 50%, and preferably at least about 75%, at least about 90%, or at least about 95% of the nucleotide residues of the first portion are capable of base pairing with nucleotide residues in the second portion. More preferably, all nucleotide residues of the first portion are capable of base pairing

with nucleotide residues in the second portion.

Similarly, Field et al (PGPUB 20040033547; para [0152]) states that:

> Sufficient complementarity occurs when a sufficient number of base pairs exist between the oligonucleotide and the target sequence to achieve detectable binding. When expressed or measured by percentage of base pairs formed, the percentage complementarity that fulfills this goal can range from as little as about 50% complementarity to full (100%) complementary. In general, sufficient complementarity is about 50%, such as about 75% complementarity, such as about 90% or 95% complementarity, such as about 98% or 100% complementarity.

Accordingly, Applicant's arguments regarding the fact that the claims encompass complementary sequences having "complete" complementarity are not persuasive because the claims do not in fact recite such a limitation.

The response states that methods of high-throughput analysis of methylation are known in the art. Applicants cite Eckhardt and Taylor for teaching methods of methylation analysis. It is argued that the invention can be practiced without undue experimentation because methods of methylation analysis are known. Applicants assert that they should not be limited to only what they have specifically exemplified.

These arguments have been fully considered but are also not persuasive. It is first noted that Applicants cannot rely on the method of Taylor to establish the predictability of detecting methylation of PITX2. Taylor 92007) is a post-filing date reference teaching "a novel approach for conducting multisample, multigene, ultradeep bisulfite sequencing analysis of DNA methylation patterns in clinical samples" (see abstract). The method disclosed by Taylor was not available at the time the invention was made. Further, neither Taylor nor Eckhardt teach the predictability of determining responsiveness to any therapy used to treat any breast cancer proliferative disorder by

assaying for hypermethylation or hypomethylation of PITX2 or a gene sharing some level of complementarity to a PITX2 gene or a gene contiguous to PITX or a gene sharing complementarity to PITX2 gene. In fact, the teachings of Eckhardt support the unpredictability of the scope of the present invention in that Eckhardt teaches that there was substantial variability in the methylation pattern of genes between different tissue, indicating the presence of tissue-specific methylation profiles (page 1382).

Applicants arguments essentially indicate that it would be within the skill of the art to assay for methylation of PITX2 or any other gene. Applicants arguments do not establish that the results of performing such assays would be predictable and would allow the artisan to practice a method of diagnosing a response to any type of therapy to any type of breast proliferative disease by detecting any change in the methylation status of any CpG in a PITX2 gene, a gene that shares some level of complementarity with the PITX2 gene or any gene upstream or downstream of the PITX2 gene. While determining the methylation pattern of a gene is within the skill of the art, it is highly unpredictable as to identity of methylation patterns that are associated with response to therapy. As discussed above, and in the rejection as set forth in the Office action of November 24, 2008, the specification does not provide sufficient information regarding the study presented there to permit one to determine if methylation of particular CpG sequences in the PITX2 gene are hypomethylated or hypermethylated in male or female patients having a particular type of breast tissue cell proliferative disorder and showing an increase or a decrease risk of relapse following a particular type of therapy. Further, the Office action establishes the unpredictability in the art of extrapolating the findings

obtained with one type of breast tissue proliferative disease to other types of breast tissue proliferative diseases, with the findings obtained regarding response to one type of therapy to other types of therapy, with the findings obtained with one tissue sample type to other tissue sample types, and with the results obtained regarding methylation status of one particular gene sequence (e.g., the promoter region of the PITX2 gene) and other sequences (3' untranslated, intron sequences, coding sequences) within that gene, genes sharing any level of complementarity thereto and genes that are upstream or downstream of the gene.

In view of the high level of unpredictability in the art, and the lack of disclosure in the specification and in the prior art, it is maintained that it would require undue experimentation for one of skill in the art to make and use the invention as broadly claimed.

Double Patenting

7. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 20-24, 45, 57-59, 61, 62, 67, and 77 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-4, 6-8, and 11-16 of copending Application No. 10/582,705. Although the conflicting claims are not identical, they are not patentably distinct from each other because the present claims and the claims of '705 are both inclusive of methods of predicting the response of a subject having a cell proliferative disorder of the breast tissue to a treatment comprising determining the methylation status of one or more CpG positions within the PITX2 gene to thereby predict a subject's response to treatment. While the claims of '705 do not define the treatment as one that target the estrogen receptor pathway or that are involved in estrogen metabolism, production or secretion and particularly do not recite that the treatment is tamoxifen, when read in light of the specification of '705 it is clear that the treatment is intended to specifically include treatments that target the estrogen receptor pathway and treatments that are involved in estrogen metabolism, production or secretion, and particularly include treatment with tamoxifen (see paras [0191], [0378] and [0476] of the PGPUB for '705, i.e., 20080254447). Further, while the claims of '705 do not specifically recite that the target sequence of the PITX2 gene comprises SEQ ID NO: 83, 411, 412, 685 or 686, the claims of '705 do include analyzing the methylation status of the target region of SEQ ID NO: 23. Since the present claims encompass methods that analyze a sequence having any level of complementarity to any contiguous portion (of any length) of SEQ ID NO:

83, 411, 412, 685 or 686, the present claims broadly encompass analyzing essentially any target region and thus encompass analyzing the same target region as claimed in '705.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response to Remarks:

In the response, Applicants state that complementary as recited in the claims refers to complete complementarity as is well known in the art. Applicants assert that the Examiner's reliance 'on "complementarity to SEQ ID NO: 23 of '705 is not reasonable supported."

This argument has been fully considered but is not persuasive. As discussed above, the term complementary is not defined in the specification or claims as being limited to sequences that share 100% complementarity. Further, as also discussed above, the term "complementary" is used in the art to indicate that sequences may share any percentage or degree of complementarity, such as 10% or 20% or 50% etc. Accordingly, Applicant's arguments are not persuasive because they are not directed to limitations recited in the claims.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carla Myers whose telephone number is 571-272-0747. The examiner can normally be reached on Monday-Thursday (6:30-5:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James (Doug) Schultz can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Carla Myers/
Primary Examiner, Art Unit 1634